## Cyclic changes that occur in the breast

## What is normal breast development?

Breast development is a vital part of a woman’s reproduction. Breast development happens in certain stages during a woman's life: first before birth, again at puberty, and later during the childbearing years. Changes also happen to the breasts during the menstrual cycle and when a woman reaches menopause.

## When does breast development begin?

Breasts begin to form while the unborn baby is still growing in the mother’s uterus. This starts with a thickening in the chest area called the mammary ridge or milk line. By the time a baby girl is born, nipples and the beginnings of the milk-duct system have formed.

Breast changes continue to happen over a woman’s life. The first thing to develop are lobes, or small subdivisions of breast tissue. Mammary glands develop next and consist of 15 to 24 lobes. Mammary glands are influenced by hormones activated in puberty. Shrinkage (involution) of the milk ducts is the final major change that happens in the breast tissue. The mammary glands slowly start to shrink. This often starts around age 35.



## What breast changes happen at puberty?

As a girl approaches her teen years, the first visible signs of breast development begin. When the ovaries start to produce and release (secrete) estrogen, fat in the connective tissue starts to collect. This causes the breasts to enlarge. The duct system also starts to grow. Often these breast changes happen at the same that pubic hair and armpit hair appear.

Once ovulation and menstruation begin, the maturing of the breasts begins with the formation of secretory glands at the end of the milk ducts. The breasts and duct system continue to grow and mature, with the development of many glands and lobules. The rate at which breasts grow is different for each young woman.

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| Female breast developmental stages | Description |
| Stage 1 | Preteen. Only the tip of the nipple is raised. |
| Stage 2 | Buds appear, and breast and nipple are raised. The dark area of skin around the nipple (the areola) gets larger. |
| Stage 3 | Breasts are slightly larger, with glandular breast tissue present. |
| Stage 4 | The areola and nipple become raised and form a second mound above the rest of the breast. |
| Stage 5 | Mature adult breast. The breast becomes rounded and only the nipple is raised. |

## What cyclical changes happen to the breasts during the menstrual cycle?

Each month, women go through changes in the hormones that make up the normal menstrual cycle. The hormone estrogen is produced by the ovaries in the first half of the menstrual cycle. It stimulates the growth of milk ducts in the breasts. The increasing level of estrogen leads to ovulation halfway through the cycle. Next, the hormone progesterone takes over in the second half of the cycle. It stimulates the formation of the milk glands. These hormones are believed to be responsible for the cyclical changes that many women feel in their breasts just before menstruation. These include swelling, pain, and soreness.

During menstruation, many women also have changes in breast texture. Their breasts may feel very lumpy. This is because the glands in the breast are enlarging to get ready for a possible pregnancy. If pregnancy does not happen, the breasts go back to normal size. Once menstruation starts, the cycle begins again.

## What happens to the breasts during pregnancy and milk production?

Many healthcare providers believe the breasts are not fully mature until a woman has given birth and made milk. Breast changes are one of the earliest signs of pregnancy. This is a result of the hormone progesterone. In addition, the dark areas of skin around the nipples (the areolas) begin to swell. This is followed by the rapid swelling of the breasts themselves. Most pregnant women feel soreness down the sides of the breasts, and nipple tingling or soreness. This is because of the growth of the milk duct system and the formation of many more lobules.

By the fifth or sixth month of pregnancy, the breasts are fully capable of producing milk. As in puberty, estrogen controls the growth of the ducts, and progesterone controls the growth of the glandular buds. Many other hormones also play vital roles in milk production. These include follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, oxytocin, and human placental lactogen (HPL).

Other physical changes happen as well. These include the blood vessels in the breast becoming more visible and the areola getting larger and darker. All of these changes are in preparation for breastfeeding the baby after birth.

## What happens to the breasts at menopause?

By the time a woman reaches her late 40s and early 50s, perimenopause is starting or is well underway. At this time, the levels of estrogen and progesterone begin to change. Estrogen levels dramatically decrease. This leads to many of the symptoms commonly linked to menopause. Without estrogen, the breast’s connective tissue becomes dehydrated and is no longer elastic. The breast tissue, which was prepared to make milk, shrinks and loses shape. This leads to the "saggy" breasts associated with women of this age.

Women who are taking hormone therapy may have some of the premenstrual breast symptoms that they had while they were still menstruating, such as soreness and swelling. But if a woman’s breasts were saggy before menopause, this will not change with hormone therapy.

**Cyclic changes in the vagina**

The **vaginal epithelium** is the inner lining of the [vagina](/wiki/Vagina%22%20%5Co%20%22Vagina) consisting of multiple layers of ([squamous](/wiki/Epithelium%22%20%5Co%20%22Epithelium)) cells. The basal membrane provides the support for the first layer of the epithelium-the basal layer. The intermediate layers lie upon the basal layer and the superficial layer is the outermost layer of the epithelium. Anatomists have described the epithelium as consisting of as many as 40 distinct layers.[*[citation needed](/wiki/Wikipedia%3ACitation_needed%22%20%5Co%20%22Wikipedia%3ACitation%20needed)*] The mucus found on the epithelium is secreted by the cervix and uterus. The rugae of the epithelium create an involuted surface and result in a large surface area that covers 360 cm3. This large surface area allows the trans-epithelial absorption of some medications via the vaginal route.

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| ***Vaginal epithelium*** |
| IMG_256The epithelium of the vagina, visible at top, consists of multiple layers of flat cells. |
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In the course of the [reproductive cycle](/wiki/Biological_life_cycle%22%20%5Co%20%22Biological%20life%20cycle), the vaginal epithelium is subject to normal, cyclic changes, that are influenced by [estrogen](/wiki/Estrogen%22%20%5Co%20%22Estrogen): with increasing circulating levels of the [hormone](/wiki/Hormone%22%20%5Co%20%22Hormone), there is proliferation of epithelial cells along with an increase in the number of cell layers. As cells proliferate and mature, they undergo partial cornification. Although hormone induced changes occur in the other tissues and organs of the female reproductive system, the vaginal epithelium is more sensitive and its structure is an indicator of estrogen levels. Some [Langerhans cells](/wiki/Langerhans_cell%22%20%5Co%20%22Langerhans%20cell) and [melanocytes](/wiki/Melanocyte%22%20%5Co%20%22Melanocyte) are also present in the epithelium. The epithelium of the [ectocervix](/wiki/Ectocervix%22%20%5Co%20%22Ectocervix) is contiguous with that of the vagina, possessing the same properties and function. The vaginal epithelium is divided into layers of cells, including the [basal cells](/wiki/Stratum_basale%22%20%5Co%20%22Stratum%20basale), the parabasal cells, the superficial [squamous flat cells](/wiki/Squamous_cell%22%20%5Co%20%22Squamous%20cell), and the intermediate cells. The superficial cells [exfoliate](/wiki/Exfoliation_corrosion%22%20%5Cl%20%22Exfoliation%22%20%5Co%20%22Exfoliation%20corrosion) continuously and basal cells replace the superficial cells that die and slough off from the [stratum corneum](/wiki/Stratum_corneum%22%20%5Co%20%22Stratum%20corneum). Under the stratus corneum is the [stratum granulosum](/wiki/Stratum_granulosum%22%20%5Co%20%22Stratum%20granulosum) and [stratum spinosum](/wiki/Stratum_spinosum%22%20%5Co%20%22Stratum%20spinosum). The cells of the vaginal epithelium retain a usually high level of glycogen compared to other epithelial tissue in the body. The surface patterns on the cells themselves are circular and arranged in longitudinal rows. The epithelial cells of the uterus possess some of the same characteristics of the vaginal epithelium.

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## Structure

Vaginal epithelium forms transverse ridges or [rugae](/wiki/Vaginal_rugae%22%20%5Co%20%22Vaginal%20rugae)that are most prominent in the lower third of the vagina. This structure of the epithelium results in an increased surface area that allows for stretching. This layer of epithelium is protective, and its uppermost surface of cornified (dead) cells are unique in that they are permeable to microorganisms that are part of the vaginal flora. [The lamina propria](/wiki/Lamina_propria%22%20%5Co%20%22Lamina%20propria) of [connective tissue](/wiki/Connective_tissue%22%20%5Co%20%22Connective%20tissue) is under the epithelium.

### **Cells**

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| --- | --- | --- | --- | --- |
| **cell type** | **Features** | **Diameter** | **Nuclei** | **Notes** |
| [basal cell](/wiki/Stratum_basale%22%20%5Co%20%22Stratum%20basale) | round to cylindrical, narrow basophilic cytoplasmic space | 12-14 μm | distinct, 8–10 μm in size | only in case of severe epithelial atrophy and in repair processes after inflammation |
| [stratum granulosum](/wiki/Stratum_granulosum%22%20%5Co%20%22Stratum%20granulosum) | part of the parabasal layer, round to longitudinal oval, cytoplasm basophilic | 20 μm | clear cell nucleus | Frequent glycogen storage, thickened cell margins and decentralized cell nucleus; Predominant cell type in menopausal women[[11]](%22%20%5Cl%20%22cite_note-%3A3-11)[[23]](%22%20%5Cl%20%22cite_note-Dutta-23)[[15]](%22%20%5Cl%20%22cite_note-Mayeaux-15)[[19]](%22%20%5Cl%20%22cite_note-%3A5-19) |
| [stratum spinosum](/wiki/Stratum_spinosum%22%20%5Co%20%22Stratum%20spinosum) | part of the parabasal layer |  |  | [[19]](%22%20%5Cl%20%22cite_note-%3A5-19)[[15]](%22%20%5Cl%20%22cite_note-Mayeaux-15)[[23]](%22%20%5Cl%20%22cite_note-Dutta-23) |
| [intermediate cell](/wiki/Intermediate_mesoderm%22%20%5Co%20%22Intermediate%20mesoderm) | oval to polygonal, cytoplasm basophilic | 30–50 μm | approx. 8 μm, decreasing core-plasma relation with increase in size | in pregnancy : barge-like with thickened cell margin ("navicular cells") |
| superficial [squamous flat cells](/wiki/Squamous_cell%22%20%5Co%20%22Squamous%20cell) | polygonal, baso- or [eosinophilic](/wiki/Eosinophilic%22%20%5Co%20%22Eosinophilic), transparent, partially [keratohyaline](/wiki/Keratohyalin%22%20%5Co%20%22Keratohyalin)granule | 50–60 microns | vesicular and slightly stainable or shrunken | [[23]](%22%20%5Cl%20%22cite_note-Dutta-23)[[15]](%22%20%5Cl%20%22cite_note-Mayeaux-15) |
| stratum corneum | exfoliate, slough off |  | become detached from the epithelium | [[17]](%22%20%5Cl%20%22cite_note-Blaustein2002-17)[[18]](%22%20%5Cl%20%22cite_note-Robboy-18)[[16]](%22%20%5Cl%20%22cite_note-Beckmann-16) |

### **Basal cells**

The basal layer of the epithelium is the most mitotically active and reproduces new cells. This layer is composed of one layer of cuboidal cells lying on top of the basal membrane.

### **Parabasal cells**

The parabasal cells include the stratum granulousum and the stratum spinosum. In these two layers, cells from the lower basal layer transition from active metabolic activity to death (apoptosis). In these mid-layers of the epithelia, the cells begin to lose their [mitochondria](/wiki/Mitochondria%22%20%5Co%20%22Mitochondria) and other cell organelles. The multiple layers of parabasal cells are polyhedral in shape with prominent nuclei.

### **Intermediate cells**

Intermediate cells make abundant glycogen and store it. [Estrogen](/wiki/Estrogen%22%20%5Co%20%22Estrogen) induces the intermediate and superficial cells to fill with [glycogen](/wiki/Glycogen%22%20%5Co%20%22Glycogen). The intermediate cells contain nuclei and are larger than the parabasal cells and more flattened. Some have identified a transitional layer of cells above intermediate layer.

### **Superficial cells**

[Estrogen](/wiki/Estrogen%22%20%5Co%20%22Estrogen) induces the intermediate and superficial cells to fill with [glycogen](/wiki/Glycogen%22%20%5Co%20%22Glycogen). Several layers of superficial cells exist that consist of large, flattened cells with indistinct nuclei. The superficial cells are exfoliated continuously.

### **Cell junctions**

The junctions between epithelial cells regulate the passage of molecules, bacteria and viruses by functioning as a physical barrier. The three types of structural adhesions between epithelial cells are: tight junctions, [adherens junctions](/wiki/Adherens_junction%22%20%5Co%20%22Adherens%20junction), and [desmosomes](/wiki/Desmosome%22%20%5Co%20%22Desmosome). "Tight junctions ([zonula occludens](/wiki/Tight_junction%22%20%5Co%20%22Tight%20junction)) are composed of [transmembrane proteins](/wiki/Transmembrane_protein%22%20%5Co%20%22Transmembrane%20protein) that make contact across the intercellular space and create a seal to restrict [transmembrane proteins](/wiki/Transmembrane_proteins%22%20%5Co%20%22Transmembrane%20proteins) difusion of molecules across the epithelial sheet. Tight junctions also have an organizing role in epithelial polarization by limiting the mobility of membrane-bound molecules between the apical and basolateral domains of the plasma membrane of each epithelial cell. Adherens junctions (zonula adherens) connect bundles of [actin filaments](/wiki/Microfilament%22%20%5Co%20%22Microfilament) from cell to cell to form a continuous adhesion belt, usually just below the microfilaments." Junction integrity changes as the cells move to the upper layers of the epidermis.

### **Mucus**

The vagina itself does not contain [mucous glands](/wiki/Mucous_gland%22%20%5Co%20%22Mucous%20gland). Though [mucus](/wiki/Mucus%22%20%5Co%20%22Mucus) is not produced by the vaginal epithelium, mucus originates from the cervix. The cervical mucus that is located inside the vagina can be used to assess fertility in ovulating women. The [Bartholin's glands](/wiki/Bartholin%27s_glands%22%20%5Co%20%22Bartholin%27s%20glands) and [Skene's glands](/wiki/Skene%27s_gland%22%20%5Co%20%22Skene%27s%20gland) located at the entrance of the vagina do produce mucus.

## Development

The epithelium of the vagina originates from three different precursors during embryonic and [fetal development](/wiki/Prenatal_development%22%20%5Co%20%22Prenatal%20development). These are the vaginal squamous epithelium of the lower vagina, the columnar epithelium of the [endocervix](/wiki/Cervical_canal%22%20%5Co%20%22Cervical%20canal), and the squamous epithelium of the upper vagina. The distinct origins of vaginal epithelium may impact the understanding of [vaginal anomalies](/wiki/Vaginal_anomalies%22%20%5Co%20%22Vaginal%20anomalies). [Vaginal adenosis](/wiki/Vaginal_adenosis%22%20%5Co%20%22Vaginal%20adenosis) is a vaginal anomaly traced to displacement of normal vaginal tissue by other reproductive tissue within the muscular layer and epithelium of the vaginal wall. This displaced tissue often contains glandular tissue and appears as a raised, red surface.

## Cyclic variations

During the luteal and follicular phases of the estrous cycle the structure of the vaginal epithelium varies. The number of cell layers vary during the days of the estrous cycle:

Day 10, 22 layers

Days 12-14, 46 layers

Day 19, 32 layers

Day 24, 24 layers

The glycogen levels in the cells is at its highest immediately before ovulation.

**Menstrual cycle**

The menstrual cycle is the regular natural change that occurs in the [female reproductive system](/wiki/Female_reproductive_system%22%20%5Co%20%22Female%20reproductive%20system)(specifically the [uterus](/wiki/Uterus%22%20%5Co%20%22Uterus) and [ovaries](/wiki/Ovary%22%20%5Co%20%22Ovary)) that makes [pregnancy](/wiki/Pregnancy%22%20%5Co%20%22Pregnancy) possible. The cycle is required for the production of [oocytes](/wiki/Oocyte%22%20%5Co%20%22Oocyte), and for the preparation of the uterus for pregnancy. The menstrual cycle occurs due to the rise and fall of [estrogen](/wiki/Estrogen%22%20%5Co%20%22Estrogen). This cycle results in the thickening of the lining of the uterus, and the growth of an [egg](/wiki/Ovum%22%20%5Co%20%22Ovum), (which is required for pregnancy). The egg is released from an ovary around day fourteen in the cycle; the thickened lining of the uterus provides [nutrients](/wiki/Nutrient%22%20%5Co%20%22Nutrient) to an embryo after [implantation](/wiki/Implantation_%28human_embryo%29%22%20%5Co%20%22Implantation%20%28human%20embryo%29). If pregnancy does not occur, the lining is released in what is known as [menstruation](/wiki/Menstruation%22%20%5Co%20%22Menstruation).

Up to 80% of women report having some symptoms during the one to two weeks prior to menstruation. Common symptoms include [acne](/wiki/Acne_vulgaris%22%20%5Co%20%22Acne%20vulgaris), tender breasts, bloating, feeling tired, irritability and mood changes. These symptoms interfere with normal life and therefore qualify as [premenstrual syndrome](/wiki/Premenstrual_syndrome%22%20%5Co%20%22Premenstrual%20syndrome) in 20 to 30% of women. In 3 to 8%, they are severe.

The first period usually begins between twelve and fifteen years of age, a point in time known as [menarche](/wiki/Menarche%22%20%5Co%20%22Menarche). They may occasionally start as early as eight, and this onset may still be normal. The average age of the first period is generally later in the [developing world](/wiki/Developing_world%22%20%5Co%20%22Developing%20world) and earlier in [developed world](/wiki/Developed_world%22%20%5Co%20%22Developed%20world). The typical length of time between the first day of one period and the first day of the next is 21 to 45 days in young women and 21 to 35 days in adults (an average of 28 days). Menstruation stops occurring after [menopause](/wiki/Menopause%22%20%5Co%20%22Menopause) which usually occurs between 45 and 55 years of age. Bleeding usually lasts around 3 to 7 days.

The menstrual cycle is governed by hormonal changes. These changes can be altered by using [hormonal birth control](/wiki/Hormonal_birth_control%22%20%5Co%20%22Hormonal%20birth%20control) to prevent pregnancy. Each cycle can be divided into three phases based on events in the ovary (ovarian cycle) or in the uterus (uterine cycle). The ovarian cycle consists of the [follicular phase](/wiki/Follicular_phase%22%20%5Co%20%22Follicular%20phase), [ovulation](/wiki/Ovulation%22%20%5Co%20%22Ovulation), and [luteal phase](/wiki/Luteal_phase%22%20%5Co%20%22Luteal%20phase)whereas the uterine cycle is divided into [menstruation](/wiki/Menstruation%22%20%5Co%20%22Menstruation), proliferative phase, and secretory phase.

Stimulated by gradually increasing amounts of [estrogen](/wiki/Estrogen%22%20%5Co%20%22Estrogen) in the follicular phase, discharges of blood (menses) flow stop, and the [lining](/wiki/Endometrium%22%20%5Co%20%22Endometrium) of the uterus thickens. [Follicles](/wiki/Ovarian_follicle%22%20%5Co%20%22Ovarian%20follicle) in the ovary begin developing under the influence of a complex interplay of hormones, and after several days one or occasionally two become dominant (non-dominant follicles shrink and die). Approximately mid-cycle, 24–36 hours after the [luteinizing hormone](/wiki/Luteinizing_hormone%22%20%5Co%20%22Luteinizing%20hormone) (LH) surges, the dominant follicle releases an [ovocyte](/wiki/Ovocyte%22%20%5Co%20%22Ovocyte), in an event called ovulation. After ovulation, the ovocyte only lives for 24 hours or less without fertilization while the remains of the dominant follicle in the ovary become a [corpus luteum](/wiki/Corpus_luteum%22%20%5Co%20%22Corpus%20luteum); this body has a primary function of producing large amounts of [progesterone](/wiki/Progesterone%22%20%5Co%20%22Progesterone). Under the influence of progesterone, the [uterine lining](/wiki/Endometrium%22%20%5Co%20%22Endometrium) changes to prepare for potential [implantation](/wiki/Implantation_%28human_embryo%29%22%20%5Co%20%22Implantation%20%28human%20embryo%29) of an embryo to establish a pregnancy. If implantation does not occur within approximately two weeks, the corpus luteum will involute, causing a sharp drop in levels of both progesterone and estrogen. The hormone drop causes the uterus to shed its lining in a process termed menstruation. Menstruation also occurs in closely related [primates](/wiki/Primate%22%20%5Co%20%22Primate)([apes](/wiki/Ape%22%20%5Co%20%22Ape) and [monkeys](/wiki/Monkeys%22%20%5Co%20%22Monkeys)).